

Claims

1. An isolated nematode persistently infected with an isolated pathogen.
2. The nematode of claim 1, wherein said pathogen expresses a detectable marker.
- 5 3. The nematode of claim 1, wherein said nematode is *Caenorhabditis elegans*.
4. The nematode of claim 1, wherein said nematode is a one-day old adult hermaphrodite or an L4 larval stage worm.
5. The nematode of claim 1, wherein said pathogen colonizes the intestine of said nematode.
- 10 6. The nematode of claim 1, wherein said pathogen is *Salmonella*.
7. The nematode of claim 6, wherein said pathogen is *Salmonellae typhimurium* strain SL1344.
8. A method of screening for a virulence factor that enables a pathogen to develop a persistent infection in a nematode, comprising the steps of:
 - 15 (a) exposing a nematode to a mutagenized pathogen;
 - (b) determining whether said mutant pathogen persistently infects said nematode, a reduction of disease in said nematode relative to that caused by the non-mutagenized pathogen indicating a mutation in a virulence factor that enables said pathogen to develop a persistent infection in said nematode; and
 - 20 (c) using said mutation as a marker for identifying said virulence factor.

9. The method of claim 8, wherein said pathogen expresses a detectable marker.
10. The method of claim 8, wherein said nematode is a one-day old adult hermaphrodite or an L4 larval stage worm.
11. The method of claim 8, wherein said pathogen colonizes the intestine of
5 said nematode.
12. The method of claim 8, wherein said pathogen is *Salmonella*.
13. The method of claim 12, wherein said pathogen is *Salmonella typhimurium* strain SL1344.
14. The method of claim 8, wherein said nematode is *C. elegans*.
- 10 15. The method of claim 8, wherein said method utilizes a salmonellae/*C. elegans* killing assay.
16. The method of claim 15, wherein said mutated pathogen causes less *C. elegans* killing than the non-mutagenized pathogen.
17. A method of screening for a compound that inhibits a persistent pathogenic
15 infection in a nematode, comprising the steps of:
- (a) providing a nematode persistently infected with a pathogen;
 - (b) contacting said persistently infected nematode with a test compound; and
 - (c) determining whether the test compound inhibits the pathogenicity of said pathogen in said persistently infected nematode.

18. The method of claim 17, wherein said pathogen expresses a detectable gene.

19. The nematode of claim 17, wherein said nematode is a one-day old adult hermaphrodite or an L4 larval stage worm.

5 20. The nematode of claim 17, wherein colonization of the intestine of said nematode by said mutated pathogen is decreased.

21. The method of claim 17, wherein said pathogen is *Salmonella*.

22. The method of claim 21, wherein said pathogen is *Salmonella typhimurium* strain SL1344.

10 23. The method of claim 17, wherein said nematode is *C. elegans*.

24. The method of claim 17, wherein said test compound is provided in a compound library.

25. The method of claim 17, wherein said test compound is a small organic compound.

15 26. The method of claim 17, wherein said test compound is a peptide, peptidomimetic, or an antibody or fragment thereof.

27. The method of claim 17, wherein said inhibition of pathogenicity is measured by a salmonellae/*C. elegans* killing assay.

28. The method of claim 27, wherein said pathogen causes less *C. elegans* killing in the presence of said test compound than in the absence of said test compound.

29. A method of screening for a virulence factor that enables a pathogen to develop a persistent infection in a nematode, comprising the steps of:

- 5 (a) exposing a nematode to a mutagenized pathogen expressing a detectable marker;
- (b) determining whether said mutant pathogen persistently infects said nematode by measuring the level of detectable marker in said nematode, where a decrease of the marker in said nematode relative to that caused by the non-mutagenized pathogen
- 10 indicates a mutation in a virulence factor that enables said pathogen to develop a persistent infection in said nematode; and
- (c) using said mutation as a marker for identifying said virulence factor.

30. A method of screening for a compound that inhibits a persistent pathogenic infection in a nematode, comprising the steps of:

- 15 (a) providing a nematode persistently infected with a pathogen expressing a detectable marker;
- (b) contacting said persistently infected nematode with a test compound; and
- (c) determining whether said pathogen persistently infects said nematode by measuring the level of detectable marker in said nematode, where a decrease of the
- 20 marker in said nematode indicates that said test compound inhibits a persistent pathogenic infection in the nematode.

31. A method of screening for a virulence factor that enables a pathogen to develop a persistent infection in a nematode, said method comprising:

- (a) exposing a nematode to a pathogen expressing a gene not normally expressed

by said pathogen;

(b) determining whether said pathogen persistently infects said nematode by measuring the level of detectable marker in said nematode, where a decrease or increase of the marker in the nematode relative to that caused by the non-mutagenized pathogen indicates a mutation in a virulence factor or a virulence factor gene that enables the pathogen to develop a persistent infection in the nematode; and

(c) using gene expressed by said pathogen as a marker for identifying said virulence factor.

32. method of claim 31, wherein said screen utilizes a salmonellae/*C. elegans* killing assay.

33. The method of claim 31, wherein said pathogen has a reduced or enhanced capacity to develop a persistent infection in *C. elegans*.

34. A method of screening for a virulence factor that enables a pathogen to develop a persistent infection in a nematode, said method comprising:

(a) exposing a nematode to a pathogen, wherein said pathogen overexpresses a pathogen gene ;

(b) determining whether the pathogen persistently infects the nematode by measuring the level of detectable marker in the nematode, where a decrease or increase of the marker in the nematode relative to that caused by the non-mutagenized pathogen indicates a mutation in a virulence factor or a virulence factor gene that enables the pathogen to develop a persistent infection in the nematode; and

(c) using the mutation or virulence factor gene as a marker for identifying the virulence factor.

35. The method of claim 34, wherein said screen utilizes a salmonellae/C. elegans killing assay.

36. The method of claim 34, wherein said pathogen has a reduced or enhanced capacity to develop a persistent infection in C. elegans.

5 37. A method of screening for a virulence factor that enables a pathogen to develop a persistent infection in a nematode, comprising:

(a) exposing a nematode to a pathogen expressing a detectable marker, the pathogen being mutagenized;

10 (b) determining whether the mutant or otherwise altered pathogen persistently infects the nematode by measuring the level of detectable marker in the nematode, where a decrease or increase of the marker in the nematode relative to that caused by the non-mutagenized pathogen indicates a mutation in a virulence factor or a virulence factor gene that enables the pathogen to develop a persistent infection in the nematode; and

(c) using the mutation for identifying the virulence factor.

15 38. A method of screening for a virulence factor that enables a pathogen to develop a persistent infection in a nematode, comprising:

(a) exposing a nematode to a pathogen expressing a detectable marker, the pathogen expressing a gene not normally expressed by the pathogen;

20 (b) determining whether the mutant or otherwise altered pathogen persistently infects the nematode by measuring the level of detectable marker in the nematode, where a decrease or increase of the marker in the nematode relative to that caused by the non-mutagenized pathogen indicates a mutation in a virulence factor or a virulence factor gene that enables the pathogen to develop a persistent infection in the nematode; and

(c) using the gene expressed by said pathogen as a marker for identifying the

virulence factor.

39. A method of screening for a virulence factor that enables a pathogen to develop a persistent infection in a nematode, comprising:

- 5 (a) exposing a nematode to a pathogen expressing a detectable marker, the pathogen overexpressing a pathogen gene;
- (b) determining whether the mutant or otherwise altered pathogen persistently infects the nematode by measuring the level of detectable marker in the nematode, where a decrease or increase of the marker in the nematode relative to that caused by the non-mutagenized pathogen indicates a mutation in a virulence factor or a virulence factor
10 gene that enables the pathogen to develop a persistent infection in the nematode; and
- (c) using the gene expressed by said pathogen as a marker for identifying the virulence factor.